



IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Attorney Docket No.: SJ-0015  
Inventors: Sorrentino and Schuetz  
Serial No.: 09/866,866  
Filing Date: May 29, 2001  
Examiner: Li, Qian J.  
Group Art Unit: 1632  
Title: Method of Identifying and/or Isolating  
Stem Cells and Prognosing Responsiveness  
to Leukemia Treatment

RECEIVED

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TECH CENTER 1600/2900

DECLARATION

1. I, Dr. Balazs Sarkadi, M.D., Ph.D. am a medical doctor affiliated with National Medical Center in Budapest, Hungary. Based upon my qualifications as set forth in the attached curriculum vitae and list of publications, I am an expert in the field of ABC transporters, especially as it pertains to the generation of antibodies to ABC transport proteins including BCRP.

2. I have reviewed the Office action issued in this case dated May 21, 2003. I have further reviewed and understand the prior art methods taught by Ross (U.S. Patent 6,313,277) and

Niman (U.S. Patent 5,563,247) as identified by the Examiner in the Office action.

3. As of the priority date of May 31, 2000 there was no method known in the art to reliably produce an isolated antibody that recognizes an extracellular portion of the ABC transporter BCRP(ABCG2) in a living cell. One of skill in this field would not have expected that conventional methods available for generating antibodies as of May 31, 2000 could be used to generate an antibody that would specifically recognize the extracellular portion of BCRP on a cell.

4. In particular, someone skilled in the field of antibody production would not have reasonably expected to be able to produce an antibody that recognizes the extracellular portion of BCRP in its natural conformation, using the prior art methods taught by Ross (U.S. Patent 6,313,277) and Niman (U.S. Patent 5,563,247), as suggested by the Examiner.

5. Ross teaches antibodies prepared against a purified protein. A purified protein can have a very different conformation than the conformation that exists when the protein is in its natural state (i.e. natural conformation). ABC transporter proteins, particularly including BCRP, adopt a very

different conformation when they are purified compared to their natural conformation imbedded in the cell membrane. With respect to the extracellular domain of BCRP, it is important to note that BCRP forms a homodimer. The BCRP homodimer would be expected to adopt a very different conformation than the monomeric purified protein or purified protein fragment. As a result, any antibody generated against a purified BCRP protein, or fragment of a BCRP protein would not be expected to recognize the extracellular domain of the BCRP protein in its natural conformation embedded in the cell membrane.

6. The Niman reference discloses a method of making an antibody to a cell surface protein by using a whole cell technique. This general technique of using whole cells as immunogens to generate antibodies to extracellular epitopes of cell membrane proteins does not work well for ABC transporters. ABC transporters, particularly those such as BCRP, are only weakly expressed and have only a few small extracellular domains which are poor targets for antibodies. Therefore, the

method for generating antibodies disclosed in Niman would not be expected to successfully generate antibodies to the extracellular domain of BCRP.

*I hereby declare that all statements herein of our own knowledge are true and that all statements made on information or belief are believed to be true; and further that these statements were made with the knowledge that willful statements and the like so made are punishable by fine or by imprisonment, or both under §1001 of Title 18 of the United States Code, and that such willful statements may jeopardize the validity of the application, any patent issuing there upon, or any patent to which this verified statement is directed.*

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Dr. Balazs Sarkadi, M.D., Ph.D.

Date: \_\_\_\_\_

## CURRICULUM VITAE

**Name:** Balázs Sarkadi, M.D., Ph.D., D.Sc.

**Occupation:** Head of Department, Scientific Deputy Director

**Address:** Home: 1121 Ágnes u. 23/b, Budapest, Hungary  
(phone: 36-1-395-1816)

Office: National Medical Center, Institute of Haematology and Immunology,  
Diószegi u. 64, 1113 Budapest, Hungary, (phone/fax: 36-1-372-4353)

**Date and place of birth:** May 30, 1948, Budapest, Hungary

**Citizenship:** Hungarian

**Family status:** Married, two children (born in 1974 and 1979)

**Education:**

- Semmelweis University Medical School, Budapest, Hungary, 1966-1972;
- M.D. degree: Budapest, 1972;
- Ph.D. degree: Hungarian Academy of Sciences, 1980;
- Doctor of Biological Sciences: Hungarian Academy of Sciences, 1986

**Postdoctoral and research appointments:**

- National Institute of Haematology and Blood Transfusion, Dept. Cell Metabolism, Budapest, 1972 - present;
- The University of Chicago, Dept. Physiology, Research Associate, 1976-77;
- The Hospital for Sick Children, Dept. Cell Biology, Visiting Associate Professor, 1982-1983;
- The University of North Carolina at Chapel Hill, Visiting Professor, 1990-91; Fulbright Visiting Professor, 2000-2001.
- Hungarian Academy of Sciences, Head of Membrane Biology Research Group, 1996-

**Teaching activities:**

- 2nd Institute of Biochemistry, Semmelweis Medical University, (courses for graduate students), 1978-81;
- Postgraduate courses in haematology and immunology, 1972 - present;
- Institute of Physiology, Semmelweis Medical University, appointment in teaching general physiology, 1985-1992;
- Full professor habilitation at Semmelweis Medical University, 1995 (biology);
- Ph. D. programs in membrane biochemistry and immunology, Semmelweis Medical University and Eotvos Lorand University, from 1994.

**Memberships:**

- International Society of Haematology;
- American Society of Biochemistry and Molecular Biology
- New York Academy of Sciences;
- American Physiological Society (corresponding member);
- International Cell Research Organization (UNESCO - ICRO panel convenor);
- Hungarian Society of Biochemistry (vice-president);
- Hungarian Biophysical Society;
- FEBS Advanced Course Committee member, 1999-2001;

**Editorial experience:**

- Haematologia, managing editor, 1978-82;
- Editor of "Genetics, Structure and Function of Blood Cells", 1980;
- Editor of Biochimica Biophysica Acta, Reviews on Biomembranes,
- Reviewer for Biochimica Biophysica Acta, Cell Calcium,
- J. Membrane Biology, Haematologia.

**Organization of Scientific Meetings:**

- International Congress of Haematology, Congress Secretary (1982);
- 20th FEBS Meeting, Secretary of Scientific Program Committee (1990);
- FEBS/ICRO Advanced Courses on "Biochemistry of Membrane Transport", 1989, 1993, 1995, 1998,
- President of the Scientific Committee, FEBS-IUBMB Congress, Budapest, 2005.

**Awards:**

- Research Awards of the Hungarian Academy of Sciences, 1982, 1986;
- Howard Hughes International Fellowship, 1995-1999; 2000-2004;
- Bela Tanko Award (Hung. Biochem. Soc.), 1995;
- Szechenyi Research Professorship, Hungary, 1997;
- Fulbright Senior Research Fellowship, 2000;
- Research Award of the Hungarian Academy of Sciences, 2003.

**Symposium or plenary lectures at International Meetings:**

- Conference on "Transport ATPases", New York Acad. Sci., New York, 1982;
- Conference on "Structure and Function of Erythrocytes" Berlin, 1986;
- Symposium on the "Regulation of Cell Volume", 2nd European Congress of Cell Biology, Budapest, 1986;
- Symposium on "Membrane Transport Enzymes", FEBS Meeting, Ljubljana, 1987;
- Symposium on "Calcium Ions and Phosphoinositides", 14th Congress of the IUB, Prague, 1988;
- ICRO Symposium on "Signals and Signal Transduction in the immune System", Eger (Hungary), 1989;
- Symposium on "Calcium Transport and Calcium Signaling", 10th FEBS Meeting, Budapest, Hungary, 1990;
- Semmelweis International Symposium on "Calcium transport and calcium pools in human platelets", Budapest, Hungary, 1992;
- Symposium and Advanced Course on "ATP-binding Cassette Transporters", Gosau, Austria, 1997;
- 25th FEBS Meeting, Symposium on Transport ATPases, Copenhagen, Denmark, 1998;
- 26th FEBS Meeting, Symposium on ABC Transporters, Nice, France, 1999;
- Plenary lecturer, International Union of Biochemistry and Molecular Biology (IUBMB) Meeting, Birmingham, UK, 2000;
- Symposium and Advanced Course on "ATP-binding Cassette Transporters", Gosau, Austria, 2003;

**Publications:** see separate list

(over 110 full papers, with a total citation number of about 4,500).

## Balazs Sarkadi - LIST OF PUBLICATIONS

### Reviews and book chapters:

1. Gárdos, G., Szász, I. Sarkadi, B.:  
Mechanism of Ca-dependent K transport in human red cells.  
In: Biomembranes: Structure and Function, (eds. G. Gárdos, I. Szász), Akadémiai Kiadó, Budapest, North Holland P.Co. Amsterdam, pp. 167-180, (1975)
2. Sarkadi, B., Tosteson, D.C.:  
Active cation transport in human red cells.  
In: Membrane Transport in Biology, Vol. 2. (eds. G. Giebisch, D.C. Tosteson, and H.H. Ussing), Springer Verlag, Berlin, pp.117-160, (1978)
3. Sarkadi, B., Enyedi, A., Szász, I., Gárdos, G.:  
Effect of calmodulin on active calcium uptake and membrane phosphorylation in inside-out red cell membrane vesicles.  
In: Genetics, Structure and Function of Blood Cells (eds. S.R. Hollan, G. Gárdos, B. Sarkadi), Pergamon Press, Akadémiai Kiadó, Budapest, pp. 181-188 (1980)
4. Szász, I., Sarkadi, B., Gárdos, G.:  
Calcium-sensitivity of calcium dependent functions in human red blood cells.  
In: Genetics, Structure and Function of Blood Cells, (eds. S.R. Hollán, G. Gárdos, B. Sarkadi), Pergamon Press, Akadémiai Kiadó, Budapest, pp. 211-222 (1980)
5. Sarkadi, B., Szebeni, J., Gárdos, G.:  
Effects of calcium on cation transport processes in inside-out red cell membrane vesicles.  
In: Membrane Transport in Erythrocytes, Alfred Benson Symposium 14. (eds. U.V. Lassen, H.H. Ussing, J.O. Wieth), Munksgaard, Copenhagen, pp. 220-231, (1980)
6. Gárdos, G., Szász, I., Sarkadi, B., Szebeni, J.:  
Various pathways for passive cation transport in red cells.  
In: Membrane Transport in Erythrocytes, Alfred Benson Symposium 14. (eds. U.V. Lassen, H.H. Ussing, J.O. Wieth), Munksgaard, Copenhagen, pp. 163-174, (1980)
7. Sarkadi, B.:  
Active calcium transport in human red cells.  
*Biochem. Biophys. Acta, Reviews on Biomembranes*, 604, 159-190, (1980)

8. Sarkadi, B., Szász, I., Gárdos, G.:  
Calcium and calmodulin in the regulation of blood cell functions.  
*Haematologia* 14, 121-136, (1981)
9. Grinstein, S., Rothstein, A., Sarkadi, B., Gelfand, E.W.:  
Responses of human lymphocytes to anisotonic media: volume-regulating behaviour.  
*Am. J. Physiol.* 246, C204-C215, (1984)
10. Sarkadi, B., and Gárdos, G.:  
Calcium-induced potassium transport in cell membranes.  
In: *Enzymes of Biological Membranes*, 2nd ed. (A. Martonosi, ed.), Vol. 3, pp. 193-234, Plenum Publ. Co. (1985)
11. Sarkadi, B., and Gárdos, G.:  
Drug actions on potassium fluxes in red cells.  
In: *The Red Cell Membrane: A Model For Solute Transport*, (B.U. Raess and G. Tunncliffe, eds.), Humana Publ. Co. (1989)
12. Sarkadi, B., Parker, C.:  
Activation of ion transport pathways by changes in cell volume.  
*Biochim. Biophys. Acta, Reviews on Biomembranes*, 1071, 407-427, (1991)
13. Homolya, L., Müller, M., Holló, Zs., Sarkadi, B.:  
Fluorescence assay for studying P-glycoprotein function at single cell level.  
In: *Fluorescence Microscopy and Fluorescent Probes*, pp. 241-245, (J. Slavik, ed.) Plenum Press, NY, (1996)
14. Sarkadi, B., Müller, M.:  
Search for specific inhibitors of the multidrug transporters.  
*Sem. Cancer Biol.* 8, 171-182 (1997)
15. Váradi, A., Tusnády, G.E., Bakos, É., Sarkadi, B.:  
Membrane topology of the human multidrug resistance-associated protein (MRP) and its homologs.  
*Cytotechnology* 27, 71-79 (1998), and In: *Multiple Drug Resistance in Cancer 2*, M. Clynes, ed., Kluwer Acad. Pub, pp. 71-80 (1998)
16. Klein, I., Sarkadi, B., Váradi, A.:  
An inventory of the human ABC proteins.  
*Biochim. Biophys. Acta*, 1461, 237-262 (1999)
17. Váradi, A., Szakács, G., Bakos, É., and Sarkadi, B.:  
P-glycoprotein and the mechanism of multidrug resistance.  
In: *Mechanism of Drug Resistance in Epilepsy – Lessons from Oncology*. John Wiley and sons, LTD, Novartis Foundation, pp. 54-68 (2002).



18. Szakács, G., and Sarkadi, B.:  
Multidrug resistance in cancer and modulation of drug effects by ABC transporters.  
In: *Molecular Pathomechanisms and New Trends in Drug Research*, Harwood Acad.  
Publ., The Netherlands, 2003.

19. Váradi, A., Tusnády, G.E., and Sarkadi, B.:  
Membrane topology of ABC transporters. In: *ABC Proteins: From Bacteria to Man*,  
Elsevier, 2003.

**Publications in international journals:**

1. Spät, A., Sarkadi, B., Intödy, Zs., Körner, A., Szántó, J.:  
Effect of renal papillary lipids and prostaglandin E-2 on corticosteroid  
production in the rat.  
*Acta Physiol. Acad. Sci. Hung.* 40, 187-199, (1971)

2. Sarkadi, B., Schubert, A.:  
Energy consumption of active sodium transport in isolated frog skin.  
*Acta Biochim. Biophys. Acad. Sci. Hung.* 7, 367-376, (1972)

3. Goldschmidt, B., Sarkadi, B., Gárdos, G., Matlár, A.:  
Platelet production and survival in cyanotic congenital heart disease.  
*Scand. J. Haematol.* 13, 110-115, (1974)

4. Szász, I., Sarkadi, B., Gárdos, G.:  
Erythrocyte parameters during induced Ca-dependent rapid K-  
efflux: optimum conditions for kinetic analysis.  
*Haematologia* 8, 143-151, (1974)

5. Sarkadi, B., Szász, I., Gárdos, G.:  
The use of ionophores for rapid loading of human red cells with  
radioactive cations for cation pump studies.  
*J. Membrane Biol.* 26, 357-370, (1976)

6. Sarkadi, B., Szász, I., Gerlóczy, A., Gárdos, G.:  
Transport parameters and stoichiometry of active calcium ion extrusion in intact  
human red cells.  
*Biochim. Biophys. Acta* 464, 93-107, (1977)

7. Schubert, A., Sarkadi, B.:  
Kinetic studies on the calcium-dependent potassium transport in  
human red blood cells.  
*Acta Biochim. Biophys. Acad. Sci. Hung.* 12, 207-216, (1977)

8. Szász, I., Sarkadi, B., Gárdos, G.:  
Mechanism of Ca-dependent selective rapid K-transport induced by propranolol in  
red cells.  
*J. Membrane Biol.* 35, 75-93, (1977)

9. Gárdos, G., Szász, I., Sarkadi, B.:  
Effect of intracellular calcium on the cation transport processes in human red cells.  
*Acta Biol. Med. Germ.* 36, 823-829, (1977)
10. Szász, I., Sarkadi, B., Gárdos, G.:  
Changes in the Ca-transport processes of red cells during cold storage in ACD.  
*Brit. J. Haematol.* 39, 559-568, (1978)
11. Szász, I., Sarkadi, B., Schubert, A., Gárdos, G.:  
Effects of lanthanum on calcium-dependent phenomena in human red cells.  
*Biochim. Biophys. Acta* 512, 331-340, (1978)
- 11/a. Szász I., Hasitz, M., Sarkadi, B., Gárdos, G.:  
Phosphorylation of the Ca-pump intermediate in intact red cells, isolated membranes  
and inside-out vesicles.  
*Mol. Cell. Biochem.* 22, 147-152 (1978)
12. Sarkadi, B., Macintyre, J.D., Gárdos, G.:  
Kinetics of active calcium transport in inside-out red cell membrane vesicles.  
*FEBS Letters* 89, 78-82, (1978)
13. Pandey, G.B., Sarkadi, B., Haas, M., Gumm, R.B., Davis, J.M., Tosteson, D.C.:  
Lithium transport pathways in human red cells.  
*J. Gen. Physiol.* 72, 233-247, (1978)
14. Sarkadi, B., Alifimoff, J.K., Gunn, R.B., Tosteson, D.C.:  
Kinetics and stoichiometry of Na-dependent Li transport in human red blood cells.  
*J. Gen. Physiol.* 72, 249-265, (1978)
15. Szász, I., Sarkadi, B., Gárdos, G.:  
Effects of drugs on the calcium-dependent rapid potassium transport in calcium-  
loaded intact red cells.  
*Acta Biochim. Biophys. Acad. Sci. Hung.* 13, 133-141 (1978)
16. Sarkadi, B., Schubert, A., Gárdos, G.:  
Effects of Ca-EGTA buffers on active calcium transport in inside-out red cell  
membrane vesicles.  
*Experientia* 35, 1045-1047, (1979)
17. Sarkadi, B., Szász, I., Gárdos, G.:  
Comments on the red blood cell calcium pump: an estimate of stoichiometry.  
*J. Membrane Biol.* 46, 183-184, (1979)
18. Sarkadi, B., Szász, I., Gárdos, G.:  
Characteristics and regulation of active calcium transport in inside-out red cell  
membrane vesicles.  
*Biochim. Biophys. Acta* 598, 326-338, (1980)

Publications of Balázs Sarkadi, page 5

19. Sarkadi, B., Enyedi, A., Gárdos, G.:  
Molecular properties of the red cell calcium pump:I. Effects of calmodulin, proteolytic digestion and drugs on the kinetics of active calcium uptake in inside-out red cell membrane vesicles.  
*Cell Calcium* 1, 287-297, (1980)
20. Enyedi, A., Sarkadi, B., Szász, I., Bot, G., Gárdos, G.:  
Molecular properties of the red cell calcium pump:II. Effects of calmodulin, proteolytic digestion and drugs on the calcium-induced membrane phosphorylation by ATP in inside-out red cell membrane vesicles.  
*Cell Calcium* 1, 299-310, (1980)
21. Sarkadi, B., Enyedi, A., Gárdos, G.:  
Metal-ATP complexes as substrates and free metal ions as activators of the red cell calcium pump.  
*Cell Calcium* 2, 449-458, (1981)
22. Szász, I., Sarkadi, B., Gárdos, G.:  
Operation of a Ca-dependent K(Rb)-transport in human lymphocytes.  
*Haematologia* 15, 83-89, (1981)
23. Marino, D., Sarkadi, B., Gárdos, G., Bolis, L.:  
Calcium-induced alkali cation transport in nucleated red cells.  
*Mol. Physiol.* 1, 295-300, (1981)
24. Enyedi, A., Sarkadi, B., Nyers, A., Gárdos, G.:  
Effects of divalent metal ions on the calcium pump and membrane phosphorylation in human red cells.  
*Biochim. Biophys. Acta* 690, 41-49, (1982)
25. Sarkadi, B., Enyedi, A., Szász, I., Gárdos, G.:  
Active calcium transport and calcium-dependent membrane phosphorylation in human peripheral blood lymphocytes.  
*Cell Calcium* 3, 163-182, (1982)
26. Sarkadi, B., Enyedi, A., Nyers, A., Gárdos, G.:  
The function and regulation of the calcium pump in the erythrocyte membrane.  
*Ann. N. Y. Acad. Sci.* 402, 329-346, (1982)
27. Enyedi, A., Sarkadi, B., Gárdos, G.:  
On the substrate specificity of the red cell calcium pump.  
*Biochim. Biophys. Acta* 687, 109-112, (1982)
28. Sarkadi, B., Enyedi, A., Faragó, A., Mászáros, G., Kremmer, T., Gárdos, G.:  
Cyclic AMP-dependent protein kinase stimulates the formation of polyphosphoinositides in lymphocyte plasma membrane.  
*FEBS Letters* 152, 195-198, (1983)

29. Enyedi, A., Faragó, A., Sarkadi, B., Szász, I., Gárdos, G.:  
Cyclic AMP-dependent protein kinase stimulates the formation of  
polyphosphoinositides in the plasma membranes of different blood cells.  
*FEBS Letters* 161, 158-162, (1983)
30. Grinstein, S., Cohen, S., Sarkadi, B., Rothstein, A.:  
Induction of 86-Rb fluxes by Ca and volume changes in thymocytes and their isolated  
membranes.  
*J. Cell. Physiol.* 116, 352-362, (1983)
31. Sarkadi, B., Mack, E., Rothstein, A.:  
Ionic events during the volume response of human peripheral blood lymphocytes to  
hypotonic media: I. Distinctions between volume-activated Cl and K conductance  
pathways.  
*J. Gen. Physiol.* 83, 497-512, (1984)
32. Sarkadi, B., Mack, E., Rothstein, A.:  
Ionic events during the volume response of human peripheral blood lymphocytes to  
hypotonic media: II. Volume- and time-dependent activation and inactivation of ion  
transport pathways.  
*J. Gen. Physiol.* 83, 513-527, (1984)
33. Sarkadi, B., Attisano, L., Grinstein, S., Buchwald, M., Rothstein, A.:  
Volume regulation of Chinese hamster ovary cells in anisoosmotic media.  
*Biochim. Biophys. Acta* 774, 159-164, (1984)
34. Enyedi, A., Faragó, A., Sarkadi, B., Gárdos, G.:  
Cyclic AMP-dependent protein kinase and Ca-calmodulin stimulate the formation of  
polyphosphoinositides in a sarcoplasmic reticulum preparation of rabbit heart.  
*FEBS Letters*, 176, 235-238, (1984)
35. Farkas, G., Enyedi, A., Sarkadi, B., Gárdos, G., Nagy, Z., Faragó, A.:  
Cyclic AMP-dependent protein kinase stimulates the phosphorylation of  
phosphatidylinositol to phosphatidylinositol-4-monophosphate in a plasma membrane  
preparation from pig granulocytes.  
*Biochem. Biophys. Res. Commun.*, 124, 871-876, (1984)
36. Sarkadi, B., Cheung, R., Mack, E., Grinstein, S., Gelfand, E.W., Rothstein, A.:  
Cation and anion transport pathways in the volume regulatory response of human  
lymphocytes to hypoosmotic media.  
*Am. J. Physiol.* 248, C480-C487, (1985)
37. Sarkadi, B., Grinstein, S., Rothstein, A., Gárdos, G.:  
Analysis of Ca-induced K transport by human erythrocytes in propionate media.  
*Acta Biochim. Biophys. Acad. Sci. Hung.*, 20, 193-202, (1985)

38. Sarkadi, B., Enyedi, A., Földes-Papp, Z., Gárdos, G.:  
Molecular characterization of the in situ red cell membrane calcium pump by limited proteolysis.  
*J. Biol. Chem.* 261, 9552-9557, (1986)
39. Enyedi, A., Sarkadi, B., Földes-Papp, Z., Monostory, S., Gárdos, G.:  
Demonstration of two distinct calcium pumps in human platelet membrane vesicles.  
*J. Biol. Chem.* 261, 9558-9563, (1986)
40. Sarkadi, B., Enyedi, A., Gárdos, G.:  
Conformational changes of the in situ red cell membrane calcium pump affect its proteolysis.  
*Biochim. Biophys. Acta*, 899, 129-133 (1987)
41. Enyedi, A., Flura, M., Sarkadi, B., Gárdos, G., Carafoli, E.:  
Maximum activity and the calcium affinity of the red cell membrane calcium pump may be regulated independently.  
*J. Biol. Chem.* 262, 6425-6430, (1987)
42. Szinnai, M., Sarkadi, B., Szász, I., Gárdos, G.:  
Volume regulatory mechanisms in human platelets.  
*Haematologia*, 21, 33-40 (1988)
43. Hunyady, L., Sarkadi, B., Cragoe, E.J., Spät, A., Gárdos, G.:  
Activation of sodium-proton exchange is not a prerequisite for Ca mobilization and aggregation in human platelets.  
*FEBS Letters*, 225, 72-76 (1987)
44. Sarkadi, B., Enyedi, A., Penniston, J.T., Verma, A.K., Dux, L., Molnár, E., Gárdos, G.:  
Characterization of membrane calcium pumps by simultaneous immunoblotting and 32-P radiography.  
*Biochim. Biophys. Acta*, 939, 40-46 (1988)
45. Újhelyi, E., Onódy, K., Minh, D.Q., Sarkadi, B., Füst, G.:  
Enhancing effect of L-interferon on the C-2 synthesis by cultured human monocytes.  
*Immunol. Letters* 15, 41-44, (1987)
46. Magócsi, M., Enyedi, A., Sarkadi, B., Gárdos, G.:  
Effects of phosphoinositides on calcium movements in human platelet membrane vesicles.  
*Biochim. Biophys. Acta*, 944, 202-212 (1988)
47. Papp, B., Sarkadi, B., Enyedi, A., Caride, A.J., Penniston, J.T., and Gárdos, G.:  
Functional domains of the in situ red cell membrane calcium pump revealed by proteolysis and monoclonal antibodies. Possible sites of regulation by calpain and acidic lipids.  
*J. Biol. Chem.*, 264, 4577-4582 (1989)

48. Tordai, A., Sarkadi, B., Görög, Gy., Gárdos, G.:  
Inhibition of the CD3-mediated calcium signal by protein kinase C activators in  
human T (Jurkat) lymphoblastoid cells.  
*Immunol. Letters*, 20, 47-52 (1989)
49. Magócsi, M., Sarkadi, B., Kovács, T., Gárdos, G.:  
Thrombin-induced activation of calcium transport pathways and their role in platelet  
functions.  
*Biochim. Biophys. Acta* 984, 88-96 (1989)
50. Kovács, T., Szász, I., Sarkadi, B., Brezanoczi, F., Gárdos, G.:  
Volume regulatory mechanisms of human granulocytes in hyposmotic  
media.  
*Acta Biochim. Biophys. Hung.* 24, 83-99 (1989)
51. Enouf, J., Bredoux, R., Bourdeau, N., Sarkadi, B., Levy-Toledano, S.:  
Further characterization of the plasma membrane- and intracellular membrane-  
associated platelet Ca-transport systems.  
*Biochem. J.* 263, 547-552 (1989)
52. Sarkadi, B., Tordai, A., Gárdos, G.: Membrane depolarization selectively inhibits  
receptor-operated calcium channels in human T (Jurkat) lymphoblasts.  
*Biochim. Biophys. Acta* 1027, 130-140 (1990)
53. Sarkadi, B., Tordai, A., Müller, M., Gárdos, G.:  
Regulation of stimulus-induced calcium transport pathways in human T (Jurkat)  
lymphoblasts.  
*Mol. Immunol.* 27, 1297-1306 (1990)
54. Kovács, T., Tordai, A., Szász, I., Sarkadi, B., Gárdos, G.:  
Membrane depolarization inhibits thrombin-induced calcium influx and aggregation  
in human platelets.  
*FEBS Letters* 266, 171-174 (1990)
55. Sarkadi, B., Tordai, A., Homolya, L., Scharff, O., Gárdos, G.:  
Calcium influx and intracellular calcium release in anti-CD3 antibody-stimulated and  
thapsigargin-treated human T lymphoblasts.  
*J. Membrane Biol.* 123, 9-21 (1991)
56. Papp, B., Enyedi, A., Kovács, T., Sarkadi, B., Wuytack, F., Thastrup, O., Gárdos,  
G., Bredoux, R., Levy-Toledano, S., Enouf, J.: Demonstration of two forms of  
calcium pumps by thapsigargin inhibition and radio-immunoblotting in platelet  
membrane vesicles.  
*J. Biol. Chem.* 266, 14593-14596 (1991)

57. Sarkadi, B., Bauzon, D., Huckle, J.R., Earp, H.S., Berry, A., Suchindran, H., Price, E.M., Olsen, J.C., Boucher, R.C., Scarborough, G.A.:  
Biochemical characterization of the cystic fibrosis transmembrane conductance regulator in normal and cystic fibrosis epithelial cells.  
*J. Biol. Chem.* 267, 2087-2095 (1992)
58. Sarkadi, B., Price, E.M., Boucher, R.C., Germann, U., Scarborough, G.A.:  
Expression of the human multidrug resistance cDNA in insect cells generates a high-activity drug-stimulated ATPase.  
*J. Biol. Chem.* 267, 4854-4858 (1992)
59. Olsen, J.C., Johnson, L.G., Stutts, J.M., Sarkadi, B., Yankaskas, J.R., Swanstrom, R., Boucher, R.C.:  
Correction of the apical membrane chloride permeability defect in polarized cystic fibrosis airway epithelia following retroviral-mediated gene transfer.  
*Human Gene Therapy* 3, 253-266 (1992)
60. Johnson, L.G., Olsen, J.C., Sarkadi, B., Moore, K.L., Swanstrom, R., Boucher, R.C.:  
Efficiency of gene transfer for restoration of normal airway epithelial function in cystic fibrosis.  
*Nature Genet.* 2, 21-25 (1992)
61. Papp, B., Enyedi, Á., Pászty, K., Kovács, T., Sarkadi, B., Gárdos, G., Magnier, C., Wuytack, F., Enouf, J.:  
Simultaneous presence of two distinct endoplasmic reticulum type calcium pump isoforms in human cells. Characterization by radio-immunoblotting and inhibition by 2,5-di-(t-butyl)-1,4-benzohydroquinone.  
*Biochem. J.* 288, 297-302 (1992)
62. Yankaskas, J.R., Haizlip, J.E., Conrad, M., Koval, D., Lazarowski, E., Paradiso, A.M., Rinehart, C.A., Sarkadi, B., Schlegel, R., Boucher, R.C.:  
Papilloma virus immortalized tracheal epithelial cells retain a well-differentiated phenotype.  
*Am. J. Physiol, Cell Physiol.* 264, C1219-C1230, (1993)
63. Papp, B., Pászty, K., Kovács, T., Sarkadi, B., Gárdos, G., Enouf, J., and Enyedi, Á.:  
Characterization of the inositol trisphosphate-sensitive and -insensitive calcium stores by selective inhibition of the endoplasmic reticulum type calcium pump isoforms in isolated platelet membrane vesicles.  
*Cell Calcium*, 14, 531-538, (1993)
64. Homolya, L., Holló, Zs., Germann, U.A., Pastan, I., Gottesman, M.M., and Sarkadi, B.:  
Fluorescent cellular indicators are extruded by the multidrug resistance protein.  
*J. Biol. Chem.* 268, 21493-21496 (1993)



65. König, T., Kapus, A., Sarkadi, B. :  
Effects of equisetin on rat liver mitochondria: evidence for inhibition of substrate anion carriers of the inner membrane.  
*J. Bioenerg. Biomembr.* 25, 537-545 (1993)
66. Kovács, T., Corvazier, E., Papp, B., Magnier, C., Bredoux, R., Enyedi, Á., Sarkadi, B., Enouf, J. :  
Controlled proteolysis of Ca-ATPases in human platelet and non-muscle cell membrane vesicles.  
*J. Biol. Chem.* 269, 6177-6184 (1994)
67. Stutts, M. J., Gabriel, S.E., Price, E.M., Sarkadi, B., Olsen, J.C., and Boucher, R.C. :  
Pyridine nucleotide redox potential modulates cystic fibrosis transmembrane regulator chloride conductance.  
*J. Biol. Chem.* 269, 8867-8874 (1994)
68. Holló, Zs., Homolya, L., Davis, C.W., and Sarkadi, B. :  
Calcein accumulation as a fluorometric functional assay of the multidrug transporter.  
*Biochim. Biophys. Acta*, 1191, 384-388 (1994)
69. Sarkadi, B., Müller, M., Homolya, L., Holló, Zs., Sepródi, J., Germann, U.A., Gottesman, M.M., Price, E., and Boucher, R.C. :  
Interaction of bioactive peptides with the human multidrug transporter.  
*FASEB Journal*, 8, 766-770 (1994)
70. Welker, E., Szabó, K., Holló, Zs., Müller, M., Sarkadi, B., Váradi, A. :  
Drug-stimulated ATPase activity of a deletion mutant of the human multidrug-resistance protein (MDR1).  
*Biochem. Biophys. Res. Comm.* 216, 602-609 (1995)
71. Müller, M., Bakos, É., Welker, E., Váradi, A., Germann, U.A., Gottesman, M.M., Morse, B., S., Roninson, I.B., Sarkadi, B. :  
Altered drug-stimulated ATPase activity in mutants of the human multidrug transporter.  
*J. Biol. Chem.* 271, 1877-1883 (1996)
72. Homolya, L., Holló, Zs., Müller, M., Mechetner, E.B., Sarkadi, B. :  
A new method for quantitative assessment of P-glycoprotein related multidrug resistance in tumor cells.  
*British J. Cancer*, 73, 849-855 (1996)
73. Holló, Zs., Homolya, L., Hegedűs, T., Sarkadi, B. :  
Transport properties of the multidrug resistance associated protein (MRP) in human tumour cells.  
*FEBS Letters*, 383, 99-104 (1996)

74. Bakos, É., Hegedűs, T., Holló, Zs., Welker, E., Tusnády, G.E., Zaman, G., Flens, M.J., Váradi, A., and Sarkadi, B.:  
Membrane topology and glycosylation of the human multidrug resistance associated protein (MRP).  
*J. Biol. Chem.* 271, 12322-12326 (1996)
75. Sarkadi, B., Müller, M., Holló, Zs.:  
The multidrug transporters - proteins of an ancient immune system.  
*Immunol. Lett.* 54, 215-219 (1996)
76. Tusnády, G.E., Bakos, É., Váradi, A., Sarkadi, B.:  
Membrane topology distinguishes a subfamily of ATP-binding cassette (ABC) transporters.  
*FEBS Letters*, 402, 1-3 (1997)
77. Bakos, É., Klein, I., Welker, E., Szabó, K., Müller, M., Sarkadi, B., and Váradi, A.:  
Characterization of the human multidrug resistance protein containing mutations in the ATP-binding cassette signature region.  
*Biochem. J.* 323, 777-783 (1997)
78. Szabó, K., Bakos, É., Welker, E., Müller, M., Goodfellow, H. R., Higgins, C. F., Váradi, A., and Sarkadi, B.:  
Phosphorylation site mutations in the human multidrug transporter (MDR1) modulate its drug-stimulated ATPase activity.  
*J. Biol. Chem.*, 272, 23165-23171 (1997)
79. Szabó, K., Welker, E., Bakos, É., Müller, M., Roninson, I., Váradi, A., and Sarkadi, B.:  
Drug-stimulated nucleotide trapping in the human multidrug transporter (MDR1): co-operation of the nucleotide binding domains  
*J. Biol. Chem.*, 273, 10132-10138 (1998)
80. Holló, Zs., Homolya, L., Hegedűs, T., Müller, M., Szakács, G., Jakab, K., Antal, F., and Sarkadi, B.:  
Parallel functional and immunological detection of human multidrug resistance proteins, P-glycoprotein and MRP1.  
*Anticancer Res.*, 18, 2981-2988 (1998)
81. Bakos, É., Evers, R., Szakács, G., Tusnády, E.G., Welker, E., Szabó, K., de Haas, M., van Deemter, L., Borst, P., Váradi, A., and Sarkadi, B.:  
Functional multidrug resistance protein (MRP) lacking the N-terminal transmembrane domain.  
*J. Biol. Chem.*, 273, 32167-32175 (1998)
82. Szakács, G., Jakab, K., Antal, F., and Sarkadi, B.:  
Diagnostics of multidrug resistance in cancer.  
*Pathology Oncology Research*, 4, 251-257 (1998)

83. Szabó, K., Szakács, G., Hegedűs, T., and Sarkadi, B.:  
Nucleotide occlusion in the human CFTR: Different patterns in the two nucleotide binding domains.  
*J. Biol. Chem.*, 274, 12209-12212 (1999)
84. Sharom, F.J. Yu, X., Lu, P., Liu, R., Chu, J.W.K, Szabó, K., Müller, M., Hose, C.D., Monks, A., Váradi, A., Seprődi, J., and Sarkadi, B. :  
Interaction of the P-glycoprotein multidrug transporter (MDR1) with high affinity peptide chemosensitizers in isolated membranes, reconstituted systems and intact cells.  
*Biochem. Pharmacol.*, 58, 571-586, (1999)
85. Ito, S., Woodland, C., Sarkadi, B., Hockmann, G., Walker, S.E., Koren, G. :  
Modeling of P-glycoprotein-involved epithelial drug transport in MDCK cells.  
*Am. J. Physiol., (Renal)* 277, F84-F96 (1999)
86. Bakos, É., Evers, R., Sinkó, E., Váradi, A., Borst, P., Sarkadi, B. :  
Interactions of the human multidrug resistance proteins MRP1 and MRP2 with organic anions. *Mol. Pharmacol.*, 57, 760-768 (2000)
87. Smith, A.J., van Helvoort, A., van Meer, G., Szabó, K., Welker, E., Szakács, G., Váradi, A., Sarkadi, B., Borst, P. :  
MDR3 P-glycoprotein a phosphatidylcholine translocase, transports several cytotoxic drugs and directly interacts with drugs as judged by interference with nucleotide trapping. *J. Biol. Chem.*, 275, 23530-23569 (2000)
88. Kern, A., Felföldi, F., Sarkadi, B., and Váradi, A. :  
Expression and characterization of the N- and C-terminal ATP-binding domains of MRP1.  
*Biochem. Biophys. Res. Commun.* 273, 913-919 (2000)
89. Bakos, É., Evers, R., Calenda, J., Tusnády, G.E., Szakács, G., Váradi, A., Sarkadi, B.:  
Characterization of the amino-terminal regions in the human multidrug resistance protein (MRP1). *J. Cell Science*, 113, 4451-4461 (2000)
90. Szakács G, Özvegy C, Bakos É, Sarkadi B, Váradi A. :  
Transition-state formation in ATPase-negative mutants of human MDR1 protein.  
*Biochem. Biophys. Res. Commun.* 276, 1314-1319 (2000).
91. Karászi, É., Jakab, K., Homolya, L., Szakács, G., Holló, Z., Telek, B., Kiss, A., Rejtő, L., Nahajevszky, S., Sarkadi, B., and Kappelmayer, J. :  
Calcein assay for multidrug resistance reliably predicts therapy response and survival rate in acute myeloid leukaemia  
*Br. J. Haematol.* 112, 308-314 (2001)
92. Szakács, G., Özvegy, Cs., Bakos, É., Sarkadi, B., and Váradi, A. :

- The role of glycine-534 and glycine-1179 of human MDR1 in drug-mediated control of ATP hydrolysis. *Biochem. J.*, 356, 71-75 (2001)
93. Özvegy, Cs. Litman, T., Szakács, G. Nagy, Z., Bates, S., Váradi, A., and Sarkadi, B.:  
Functional characterization of the human multidrug transporter, ABCG2, expressed in insect cells.  
*Biochem. Biophys. Res. Commun.*, 285, 111-117 (2001)
94. Szakács, G., Langmann, T., Özvegy, Cs., Orsó, E., Schmitz, G., Váradi, A., and Sarkadi, B.:  
Characterization of the ATPase cycle of human ABCA1: implications for its function as a regulator rather than an active transporter.  
*Biochem. Biophys. Res. Commun.*, 288, 1258-1264 (2001)
95. Connolly, L., Moran, E., Larkin, A., Scheffer, G., Scheper, R., Sarkadi, B., Kool, M., Clynes, M.:  
A new monoclonal antibody, P2A8(6), that specifically recognizes a novel epitope on the Multidrug Resistance-Associated Protein 1 (MRP1), but not on MRP2 nor MRP3.  
*Hybrid Hybridomics*, 20, 333-341 (2001)
96. Hegedűs, T., Órfi, L., Seprődi, A., Váradi, A., Sarkadi, B., Kéri, G.:  
Interaction of tyrosine kinase inhibitors with the human multidrug transporter proteins, MDR1 and MRP1.  
*Biochim. Biophys. Acta*, 1587, 318-325 (2002)
97. Níás, A., Urbán, Z., Le Sanx, O., Seidl, T.L., Sinkó, E., Boyd, C.D., Sarkadi, B., and Váradi, A.:  
Loss of ATP-dependent transport activity in pseudoxanthoma elasticum-associated mutants of human ABCC6 (MRP6)  
*J. Biol. Chem.*, 277, 16860-16867 (2002)
98. Özvegy C, Váradi A, Sarkadi B.:  
Characterization of drug transport, ATP hydrolysis and nucleotide trapping by the human ABCG2 multidrug transporter: modulation of substrate specificity by a point mutation. *J. Biol. Chem.* 277, 47980-47990 (2002)
99. Bodó, A., Bakos, É, Szeri, F., Váradi, A., and Sarkadi, B.:  
The role of multidrug transporters in drug availability, metabolism and toxicity.  
*Toxicol. Letters*, 140-141, 133-143 (2003)
100. Ujhelly, O., Özvegy, Cs., Várady, G. Cervenak, J., Homolya, L., Grez, M., Scheffer, G., Roos, D., Bates, S.R., Váradi, A., Sarkadi B., and Németh, K.:  
Application of a human multidrug transporter (ABCG2) variant as selectable marker in gene transfer to progenitor cells.  
*Human Gene Therapy*, 14, 403-412 (2003)

101. Hegedűs T, Sessler, T., Scott, R., Thelin, W., Bakos, E., Váradi, A., Szabó, K., Homolya, L., Milgram, S.L., Sarkadi, B. :  
C-terminal phosphorylation of MRP2 modulates its interaction with PDZ proteins.  
*Biochem. Biophys. Res. Commun.* 302, 454-461 (2003)
102. Bodó, A., Bakos, É., Szeri, F., Váradi, A., Sarkadi B. :  
Differential modulation of the human liver conjugate transporters MRP2 and MRP3  
by bile acids and organic anions.  
*J. Biol. Chem.* 278, 23529-23537 (2003)
103. Sinkó, E., Iliás, A., Ujhelly, O., Homolya, L., Scheffer, G.L., Bergen A.A.,  
Sarkadi, B., Váradi, A.:  
Subcellular localization and N-glycosylation of human ABCC6, expressed in  
MDCKII cells.  
*Biochem. Biophys. Res. Commun.* 308, 263-269 (2003)
104. Homolya, L., Váradi, A., Sarkadi, B.:  
Multidrug resistance-associated proteins: Export pumps for conjugates with  
glutathione, glucuronate or sulfate.  
*Biofactors* 17, 103-114 (2003)
- Özvegy, Cs., Hegedűs, T., Várady, Gy. Ujhelly, O., Schuetz, J.D., Váradi, A., Kéri, G.  
Német, K., and Sarkadi, B.  
High-affinity interaction of tyrosine kinase inhibitors with the ABCG2 multidrug  
transporter.  
Manuscript prepared for Cancer Research (2003).

#### Patents:

Compounds for Reversing Drug Resistance,  
(Sarkadi, B., Seprődi, J., Csuka, O., Magócsi, M., Mező, I., Pályi, I., Teplán, I.,  
Vadász, Zs., Vincze, B.);  
Hungarian patent 215 132 (08/11/1998 - appl. number: P 92 03674; filed November  
24, 1992); PCT/TB94/00144, application filed on May 12, 1994, WO 95/31474.

2. Assay for Multidrug Resistance  
(Sarkadi, B., Homolya, L., Holló, Zs.)  
US Patent Number: 5,872,014, Date of Patent: February 16, 1999.

3. Assay and Reagent Kit for the Quantitative In Vitro Determination in Biological  
Specimens of the Activity of Proteins Causing Multidrug Resistance in Tumors.  
(Sarkadi, B., Homolya, L., Holló, Zs.)  
Hungarian patent (appl. number: P 94 02551, August 31, 1994; PCT/ HU95/00042,  
August 31, 1995); PCT: WO 96/06945, International publication date: March 7, 1996;  
European Patent: EP 0 784 699 B1 (23/07/1997).